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Paper No.: _____

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Inventor: Dong HUANG and Dong Feng QI
Title: NOVEL DAMMARANE SAPOGENINS,
THEIR USE AS ANTI-CANCER AGENTS,
AND A PROCESS FOR PRODUCING SAME
Filed: Herewith
Date: 18 October 2001

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To: Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

**LIST OF PATENTS AND PUBLICATIONS FOR
APPLICANT'S INFORMATION DISCLOSURE STATEMENT
[Form PTO-1449 (Modified)]**

United States Patent Documents

Examiner	ID	Patent No.	Issue Date	Inventor(s)	Class	Sub-Class	Filing Date
1	AA	4,157,894	June 12/79	Bambardelli			
502	AB	5,919,770	July 6/99	Hideo et al.			
1	AC	4,621,137	Nov. 4/86	Miyake et al.			
/	AD						
/	AE						
/	AF						
/	AG						
/	AH						
/	AI						
/	AJ						
/	AK						

Foreign Patent Documents

Examiner	ID	Publn. No.	Publn. Date	Country/Inventor	Class	Sub-Class	Translation?
502	BA	8-208688	Aug. 13/96	Japan - Keizo et al.			
502	BB	11-295310	Oct. 29/99	Japan - Hiroyuki et al.			

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10/19/01

152	BC	WO/97/31933	Sept. 4/97	PCT - Cheil Je Dang Co.			
	BD						
	BE						
	BF						
	BG						
	BH						
	BI						
	BJ						
	BK						

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Other Art

Examiner	ID	Author, Title, Date, Pertinent Pages, etc.
	CA	Y.S. Kim, et al., Ginsenoside Rh2 and Rh3 induce differentiation of HL-60 cells into granulocytes: modulation of protein kinase C isoforms during differentiation by ginsenoside Rh2, <i>The International Journal of Biochemistry & Cell Biology</i> 30 (1998) 327-338.
	CB	A.S. Attele, et al., Ginseng Pharmacology: Multiple Constituents and Multiple Actions, <i>Biochemical Pharmacology</i> , Vol. 58, pp. 1685-1693, 1999.
	CC	H. Hasegawa, et al., Reversal of Daunomycin and Vinblastine Resistance in Multidrug-Resistant P388 Leukemia <i>in vitro</i> through Enhanced Cytotoxicity by Triterpenoids, <i>Planta Med.</i> 61 (1995) 409-413.
	CD	www.herbmed.org/herbs/panax.htm , Alternative Medicine Foundation - information regarding ginseng.
50	CE	Abstract - Y.N. Lee, et al., In vitro induction of differentiation by ginsenosides in F9 teratocarcinoma cells, <i>Eur. J. Cancer</i> 1996, July; 32A(8):1420-8.
	CF	Abstract - S. Odashima, et al., Control of phenotypic expression of cultured B16 melanoma cells by plant glycosides, <i>Cancer Res.</i> 1985 June; 45(6):2781-4.
	CG	Abstract - L.J. Xia & R. Han, [Differentiation of B16 melanoma cells induced by ginsenoside RH2], <i>Yao Hsueh Hsueh Pao</i> 1996;31(10):742-5.
	CH	Abstract - Y. Kikuchi, et al., Inhibition of human ovarian cancer cell proliferation in vitro by ginsenoside Rh2 and adjuvant effects to cisplatin in vivo, <i>Anticancer Drugs</i> 1991 Feb;2(1):63-7.
	CI	Abstract - K.Y. Lee, et al., Ginsenoside-Rh2 blocks the cell cycle of SK-HEP-1 cells at the G1/S boundary by selectively inducing the protein expression of p27kip1, <i>Cancer Lett.</i> 1996 Dec 20; 110(1-2):193-200.
	CJ	Abstract - M. Oh, et al., Anti-proliferating effects of ginsenoside Rh2 on MCF-7 human breast cancer cells, <i>Int. J. Oncol.</i> 1999 May; 14(5):869-75.
	CK	Abstract - T. Ota, et al., G1 phase-specific suppression of the Cdk2 activity by ginsenoside Rh2 in cultured murine cells, <i>Life Sci.</i> 1997; 60(2):PL39-44.
	CL	Abstract - H. Nakata, et al., Inhibitory effects of ginsenoside Rh2 on tumor growth in nude mice bearing human ovarian cancer cells, <i>Jpn. J. Cancer Res.</i> 1998 July; 89(7):733-40.

	CM	Abstract - H.E. Kim, et al., Ginsenoside RH-2 induces apoptotic cell death in rat C6 glioma via a reactive oxygen- and caspase-dependent but Bcl-X(L)-independent pathway, <i>Life Sci.</i> 1999; 65(3):PL33-40.
	CN	Abstract - J.A. Park, et al., Activation of caspase-3 protease via a Bcl-2-insensitive pathway during the process of ginsenoside Rh2-induced apoptosis, <i>Canc. Lett.</i> 1997 Dec 16; 121(1):73-81.
	CO	Abstract - K. Shinkai, et al., Inhibition of in vitro tumor cell invasion by ginsenoside Rg3, <i>Jpn. J. Cancer Res.</i> 1996 Apr. 87(4):357-62.
	CP	Abstract - H. Iishi, et al., Inhibition by ginsenoside Rg3 of bombesin-enhanced peritoneal metastasis of intestinal adenocarcinomas induced by azoxymethane in Wistar rats, <i>Clin. Exp. Metastasis</i> 1997 Nov; 15(6):603-11.
	CQ	Abstract - M. Mochizuki et al., Inhibitory effect of tumor metastasis in mice by saponins, ginsenoside-Rb2, 20(R)- and 20(S)-ginsenoside-Rg3, of red ginseng, <i>Biol. Pharm. Bull.</i> 1995 Sep.;18(9):1197-202.
	CR	Abstract - Lee, S.J., et al., Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin, <i>Cancer Lett.</i> 1999 Sep. 20; 144(1):39-43.
SEA	CS	Abstract - M. Yoshikawa, et al., Bioactive saponins and glycosides. XI. Structures of new dammarane-type triterpene oligoglycosides, quinquenosides I, II, III, IV, and V, from American ginseng, the roots of <i>Panax quinquefolium</i> L., <i>Chem. Pharm. Bull.</i> (Tokyo) 1998 Apr.; 46(4):647-54.
	CT	Abstract - A.M. Popov, et al., [Comparative study of anti-tumor activity of the monoglucosides protopanaxadiol and betulafolientriol], <i>Antibiot. Khimioter</i> 1994 Jul.;39(7):24-9.
	CU	Abstract - T. Kaku et al., Chemico-pharmacological studies on saponins of <i>Panax ginseng</i> C.A. Meyer. II. Pharmacological Part, <i>Arzneimittelforschung</i> 1975 Apr.; 25(4):539-47.
	CV	Abstract - Y.S. Kim, et al., Ginsenoside Rh2 and Rh3 induce differentiation of HL-60 cells into granulocytes: modulation of protein kinase C isoforms during differentiation by ginsenoside Rh2, <i>Int. J. Biochem. Cell Biology</i> 1998 Mar.;30(3):327-38.
	Cw	Abstract - Y. Takino, [Studies on the pharmacodynamics of ginsenoside-Rg1, -Rb1 and -Rb2 in rats], <i>Yakugaku Zasshi</i> 1994 Aug.;114(8):550-64. (Also list of titles of related articles.)
	CX	Abstract - N.M. Duc, et al., Saponins from Vietnamese ginseng, <i>Panax vietnamensis</i> Ha et Grushv. collected in central Vietnam. III. <i>Chem. Pharm. Bull.</i> (Tokyo) 1994 Mar.;42(3):634-40.
	CY	Abstract - N.I. Baek, et al., Ginsenoside Rh4, a genuine dammarane glycoside from Korean red ginseng, <i>Planta Med.</i> 1996 Feb.;62(1):86-7.
	CZ	Abstract - M. Yoshikawa, et al., Bioactive saponins and glycosides. VIII. Notoginseng (1): new dammarane-type triterpene oligoglycosides, notoginsenosides-A, -B, -C and -D, from the dried root of <i>Panax notoginseng</i> (Burk.) F.H. Chen. <i>Chem. Pharm. Bull.</i> (Tokyo) 1997 June;45(6):1039-45.
	DA	Abstract - D. Hou, et al., Separation and determination of chemical constituents in the volatile oil of three traditional Chinese crude drugs, <i>J. Pharm. Biomed. Anal.</i> 1998 Sept.;17(8):1423-6.
	DB	Abstract - J.P. Hou, The chemical constituents of ginseng plants, <i>Comp. Med. East West</i> 1977 Summer;5(2):123-45.

	DC	Abstract - J.F. Cui, et al., Gas chromatographic-mass spectrometric determination of 20(S)-protopanaxadiol and 20(S)-protopanaxatriol for study on human urinary excretion of ginsenosides after ingestion of ginseng preparations, <i>J. Chromatogr. B. Biomed. Sci. App.</i> 1997 Feb. 21;689(2):349-55.
	DD	Abstract - J.F. Cui, et al., Analysis of ginsenosides by chromatography and mass spectrometry: release of 20 S-protopanaxadiol and 20 S-protopanaxatriol for quantitation, <i>Anal. Biochem.</i> 1993 May 1;210(2):411-7.
	DE	Abstract - T. Ota, et al., Mechanism of action of ginsenoside Rh2: uptake and metabolism of ginsenoside Rh2 by cultured B16 melanoma cells, <i>J. Pharm. Sci.</i> 1991 Dec.;80(12):1141-6.
	DF	Abstract - C. Wakabayashi, et al., An intestinal bacterial metabolite of ginseng protopanaxadiol saponins has the ability to induce apoptosis in tumor cells, <i>Biochem. Biophys. Res. Commun.</i> 1998 May 29;246(3):725-30.
	DG	Abstract - C. Wakabayashi, et al., In vivo antimetastatic action of ginseng protopanaxadiol saponins is based on their intestinal bacterial metabolites after oral administration. <i>Oncol. Res.</i> 1997;9(8):411-7.
<i>S.O.B.</i>	DH	Abstract - S.J. Lee, et al., Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin, <i>Cancer Lett.</i> 1999 Sep. 20;144(1):39-43.
	DI	Abstract - H. Hasegawa & M. Uchiyama, Antimetastatic efficacy of orally administered ginsenoside Rb1 in dependence on intestinal bacterial hydrolyzing potential and significance of treatment with an active bacterial metabolite, <i>Planta Med.</i> 1998 Dec.;64(8):696-700.
	DJ	Abstract - K. Okita, et al., Anti-growth effects with components of Sho-saiko-to (TJ-9) on cultured human hepatoma cells, <i>Eur. J. Cancer Prevention</i> 2(2):169-75, 1993 Mar.
	DK	Abstract - A.S. Attele, et al., Ginseng pharmacology: multiple constituents and multiple actions, <i>Biochemical Pharmacology.</i> 58(11):1685-93, 1999 Dec. 1.
	DL	Abstract - M. Oh, et al., Anti-proliferating effects of ginsenoside Rh2 on MCF-7 human breast cancer cells, <i>International Journal of Oncology</i> , 14(5):869-75, 1999 May.
	Dm	Abstract - J. Molnar, et al., Membrane associated antitumor effects of crocine-, ginsenoside- and cannabinoid derivatives, <i>Anticancer Research</i> 20(2A):861-7, 2000 Mar.-Apr.
	DN	Abstract - M. Mochizuki, et al., Inhibitory effect of tumor metastasis in mice by saponins, ginsenoside-Rb2, 20(R)- and 20(S)-ginsenoside-Rg3 of red ginseng, <i>Biological & Pharmaceutical Bulletin</i> , 18(9):1197-202, 1995 Sep.
	DO	www.rxlist.com/cgi/alt/ginseng.htm - article regarding ginseng.
	DP	online.daylight.com - print-outs showing chemical structures of panaxadiol, protopanaxadiol, protopanaxatriol, 20(R)-ginsenoside-h2, 20(S)-ginsenoside-Rh2, Dammara-20,24-dien-3beta-ol and Betalafolien(e)triol.
	DQ	

Examiner: *S.O.B.*

Date Considered: *2/7/03 S.O.B.*

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